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FILE 'HOME' ENTERED AT 14:23:21 ON 11 JUL 2003

L1 QUE (PATHOGEN OR BACTER#### OR VIRUS) (S) ((DEVELOPEMENT## OR DEVELOPMENT##) (A) (DISORDER) OR AUTISM OR PDD)

L2 169 (PATHOGEN OR BACTER#### OR VIRUS) (S) ((DEVELOPEMENT## OR DEVELOPMENT##) (A) (DISORDER) OR AUTISM OR PDD)

L9 7 L8 AND (DIAGNOSE OR DETERMINE) (S) ((DEVELOPEMENT## OR DEVELOPMENT##) (A) DISORDER OR AUTISM OR PDD)

L10 18 L8 AND (DIAGNOS## OR DETERMIN#####) (S) ((DEVELOPEMENT## OR DEVELOPMENT##) (A) DISORDER OR AUTISM OR PDD)

L11 24 L7 AND (DIAGNOS## OR DETERMIN#####) (S) ((DEVELOPEMENT## OR DEVELOPMENT##) (A) DISORDER OR AUTISM OR PDD)

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(FILE 'HOME' ENTERED AT 14:23:21 ON 11 JUL 2003)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 14:23:46 ON 11 JUL 2003

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12	FILE ADISCTI
19	FILE ADISNEWS
2	FILE AGRICOLA
1	FILE AQUASCI
1	FILE BIOBUSINESS
1	FILE BIOCOMMERCE
96	FILE BIOSIS
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169	FILE BIOTECHDS
24	FILE BIOTECHNO
19	FILE CABA
15	FILE CANCERLIT
26	FILE CAPLUS
1	FILE CONFSCI
2	FILE DDFB
3	FILE DDFU
3212	FILE DGENE
2	FILE DRUGB
10	FILE DRUGU
1	FILE EMBAL
68	FILE EMBASE
32	FILE ESBIOBASE
22*	FILE FEDRIP
1	FILE FROSTI
1	FILE FSTA
1	FILE GENBANK
1	FILE HEALSAFE
10	FILE IFIPAT
9	FILE JICST-EPLUS
30	FILE LIFESCI
36	FILE MEDLINE

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                2   FILE NIOSHTIC
                2   FILE NTIS
               34   FILE PASCAL
                1   FILE PHARMAML
                7   FILE PHIN
               18   FILE PROMT
               67   FILE SCISEARCH
               25   FILE TOXCENTER
              194   FILE USPATFULL
                3   FILE USPAT2
                1   FILE VETU
              172   FILE WPIDS
              172   FILE WPINDEX
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L2          169 S L1
L3          169 DUP REM L2 (0 DUPLICATES REMOVED)
L4          169 S L3
L5           14 S L3 NOT PY>2000

     FILE 'MEDLINE, CAPLUS, BIOSIS, BIOTECHNO, EMBASE, SCISEARCH' ENTERED AT
     14:31:48 ON 11 JUL 2003
L6          317 S L1
L7          152 DUP REM L6 (165 DUPLICATES REMOVED)
L8           89 S L7 NOT PY>2000
L9            7 S L8 AND (DIAGNOSE OR DETERMINE) (S) ((DEVELOPEMENT## OR DEVEL
L10          18 S L8 AND (DIAGNOS## OR DETERMIN#####) (S) ((DEVELOPEMENT## OR
L11          24 S L7 AND (DIAGNOS## OR DETERMIN#####) (S) ((DEVELOPEMENT## OR
L12           6 S L11 NOT L10

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L10 ANSWER 2 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:457217 BIOSIS
DN PREV200000457217
TI Enterocolitis in children with developmental disorders.
AU Wakefield, A. J. (1); Anthony, A.; Murch, S. H.; Thomson, M.; Montgomery, S. M.; Davies, S.; O'Leary, J. J.; Berelowitz, M.; Walker-Smith, J. A.
CS (1) Inflammatory Bowel Disease Study Group, Department of Medicine, Royal Free and University College Medical School, Hampstead, Royal Free Campus, London, NW3 2QG UK
SO American Journal of Gastroenterology, (September, 2000) Vol. 95, No. 9, pp. 2285-2295. print.
ISSN: 0002-9270.
DT Article
LA English
SL English
AB OBJECTIVE: Intestinal pathology, i.e., ileocolonic lymphoid nodular hyperplasia (LNH) and mucosal inflammation, has been described in children with **developmental disorders**. This study describes some of the endoscopic and pathological characteristics in a group of children with **developmental disorders** (affected children) that are associated with behavioral regression and bowel symptoms, and compares them with pediatric controls. METHODS: Ileocolonoscopy and biopsy were performed on 60 affected children (median age 6 yr, range 3-16; 53 male). Developmental **diagnoses** were **autism** (50 patients), Asperger's syndrome (five), disintegrative disorder (two), attention deficit hyperactivity disorder (ADHD) (one), schizophrenia (one), and dyslexia (one). Severity of ileal LNH was graded (0-3) in both affected children and 37 developmentally normal controls (median age 11 yr, range 2-13 yr) who were investigated for possible inflammatory bowel disease (IBD). Tissue sections were reviewed by three pathologists and scored on a standard proforma. Data were compared with ileocolonic biopsies from 22 histologically normal children (controls) and 20 children with ulcerative colitis (UC), scored in an identical manner. Gut **pathogens** were sought routinely. RESULTS: Ileal LNH was present in 54 of 58 (93%) affected children and in five of 35 (14.3%) controls ($p < 0.001$). Colonic LNH was present in 18 of 60 (30%) affected children and in two of 37 (5.4%) controls ($p < 0.01$). Histologically, reactive follicular hyperplasia was present in 46 of 52 (88.5%) ileal biopsies from affected children and in four of 14 (29%) with UC, but not in non-IBD controls ($p < 0.01$). Active ileitis was present in four of 51 (8%) affected children but not in controls. Chronic colitis was identified in 53 of 60 (88%) affected children compared with one of 22 (4.5%) controls and in 20 of 20 (100%) with UC. Scores of frequency and severity of inflammation were significantly greater in both affected children and those with UC, compared with controls ($p < 0.001$). CONCLUSIONS: A new variant of inflammatory bowel disease is present in this group of children with **developmental disorders**.

L10 ANSWER 5 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:39700 BIOSIS
DN PREV200000039700
TI Gastrointestinal abnormalities in children with autistic disorder.
AU Horvath, Karoly (1); Papadimitriou, John C.; Rabsztyn, Anna; Drachenberg, Cinthia; Tyson Tildon, J.
CS (1) Department of Pediatrics, 22 S Greene St, N5W70, Baltimore, MD, 21201-1595 USA
SO Journal of Pediatrics, (Nov., 1999) Vol. 135, No. 5, pp. 559-563.
ISSN: 0022-3476.
DT Article

LA English
SL English
AB Objectives: Our aim was to evaluate the structure and function of the upper gastrointestinal tract in a group of patients with **autism** who had gastrointestinal symptoms. Study design: Thirty-six children (age: 5.7 +- 2 years, mean +- SD) with autistic disorder underwent upper gastrointestinal endoscopy with biopsies, intestinal and pancreatic enzyme analyses, and **bacterial** and fungal cultures. The most frequent gastrointestinal complaints were chronic diarrhea, gaseousness, and abdominal discomfort and distension. Results: Histologic examination in these 36 children revealed grade I or II reflux esophagitis in 25 (69.4%), chronic gastritis in 15, and chronic duodenitis in 24. The number of Paneth's cells in the duodenal crypts was significantly elevated in autistic children compared with non-autistic control subjects. Low intestinal carbohydrate digestive enzyme activity was reported in 21 children (58.3%), although there was no abnormality found in pancreatic function. Seventy-five percent of the autistic children (27/36) had an increased pancreatico-biliary fluid output after intravenous secretin administration. Nineteen of the 21 patients with diarrhea had significantly higher fluid output than those without diarrhea. Conclusions: Unrecognized gastrointestinal disorders, especially reflux esophagitis and disaccharide malabsorption, may contribute to the behavioral problems of the non-verbal autistic patients. The observed increase in pancreatico-biliary secretion after secretin infusion suggests an upregulation of secretin receptors in the pancreas and liver. Further studies are required to **determine** the possible association between the brain and gastrointestinal dysfunctions in children with autistic disorder.

L10 ANSWER 7 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1998:258432 BIOSIS
DN PREV199800258432
TI Bovine virus diarrhoea. Review article.
AU Kecskemeti, S. (1); Kiss, I.
CS (1) Debreceni Allat-egeszsegugyi Intezet, Bornemissza u. 3-5, H-4031 Debrecen Hungary
SO Magyar Allatorvosok Lapja, (March, 1998) Vol. 120, No. 3, pp. 143-151. ISSN: 0025-004X.
DT Article
LA Hungarian
SL Hungarian; English
AB The infection caused by bovine diarrhoea **virus** (BVDV) generally causes mild clinical symptoms in immunocompetent cattle. A severe disease can be observed mainly in young animals. The infection of pregnant animals is especially important because the **virus** may invade the fetus. Due to an infection caused by a non-cytopathogenic BVDV strain persistently infected, immunotolerant animals may be born which are consistently viraemic and can shed the **virus** during the whole lifetime, Such an infection can not be caused by a cytopathogenic biotype. **Developmental disorders** of central nervous system and eyes may develop in case of an infection between the 90th and 150th days of pregnancy. The fetus is able to produce antibodies against the **virus** during the second half of pregnancy. Venereal infections are also important. Bulls - in case of an acute infection with lower titres and for a shorter period, however in case of persistent infections persistently and with a higher titre - shed the **virus** . The **virus** in the semen may cause seroconversion, return to heat, embryonic disorders, etc. in the infected animals and the animals born can be persistently infected. Mucosal disease (MD) may develop in animals persistently infected with a non-cytopathogenic BVDV during the

fetal life - between the 40th and 120th days - when the animals are super infected with a cytopathogenic BVDV later on. When the super infecting **virus** has a homologous antigenic structure a disease develops with low morbidity but high mortality. When the antigenic structure of the super infecting **virus** is partly heterologous, due to the antibodies produced against it the super infecting **virus** disappear from the blood. MD develops weeks or months after the super infection. MD does not develop after a super infection with homologous or heterologous cytopathogenic BVDV, even antibodies are produced against the heterologous **virus**. **Diagnosis** of the diseases caused by BVDV is based on the clinical symptoms, pathological and histological alterations and results of laboratory investigations. Demonstration of the **virus**, **virus** antigen or nucleic acid are used for the laboratory **diagnosis** of BVDV.

L10 ANSWER 8 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1995:228097 BIOSIS
DN PREV199598242397
TI Prevalence of hepatitis B virus markers in several institutions for the mentally handicapped in the autonomous community of Madrid.
AU Carrascosa, Diana; De La Vega Ramirez, M.; Casado, Angela; Je La Torre, M. Roserio; Lopezfernandez, M. Encarnacion; Saez, Julia
CS Departamento de Fisiopatologia y Genetica Molecular Humana, Centro di Investigaciones Biologicas, c. Velazquez 144, 28006-Madrid Spain
SO American Journal of Human Biology, (1995) Vol. 7, No. 2, pp. 217-222. ISSN: 1042-0533.
DT Article
LA English
AB In order to **determine** the prevalence of hepatitis B **virus** (HBV) markers, 400 patients were studied: 134 residents of an institution (RI) for the mentally retarded and 266 under non-residential care (NRC). In the residential institutions, all markers were absent in 69 (65.7%) of 105 patients with Down syndrome and 20 (69.0%) of 29 clients without Down syndrome. In the NRC clients, 167 (85.6%) of 195 patients with Down syndrome and 65 (91.5%) of 71 clients with other mental defects (psychologically and physically handicapped, **autism**) had negative tests for HBV markers. The prevalence of the hepatitis B surface antigen (HBsAg) was higher in institutionalized mentally retarded (RI) and older patients (21+ years). Examination of 195 Down patients revealed a higher frequency (1.4 times) of surface antigen carriers as strictly matched nonDown syndrome cases (point prevalences 14.2% and 10.3%, respectively). The higher prevalence in affected cases appears to be primarily associated with a longer persistence of antigenemia. Results related to the sex of the patients were less clear. Neither affected nor non-affected patients showed significant differences in prevalence among males and females.

L10 ANSWER 10 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1993:505907 BIOSIS
DN PREV199396129914
TI Infantile autism in Nordland County: Prevalence and etiology.
AU Herder, Gyro Aas
CS Barneavdelingen, Nordland Sentralsykehus, 8017 Bodo Norway
SO Tidsskrift for den Norske Laegeforening, (1993) Vol. 113, No. 18, pp. 2247-2249.
ISSN: 0029-2001.
DT Article
LA Norwegian
SL Norwegian; English
AB Few epidemiological studies of infantile **autism** have been

conducted in Norway. A prevalence of four per 100 000 children was found in Nord-Trondelag. Studies from Sweden, England and Japan show prevalence figures of 2-13 per 10 000. Causal factors of **autism** are complicated, but many studies in recent years indicate that both genetic and neurological factors are important. The aim of this study was to establish the prevalence of infantile **autism** in Nordland County look for casual factors and disabilities among the children. Together with the **Autism** Team we found 28 persons, born between 1975 and 1991, who lived in the county in 1992. This gives a prevalence of 5.5 per 10 000. 21 were boys, seven girls. 26 were mentally retarded, 13 had no verbal speech. Nine had epilepsy. 13 children were **diagnosed** before the age of four. Different diseases and impairments associated with **autism** were discovered in all 19 children. In the case of eight children we found associated disease. When a **diagnosis** of infantile **autism** is made, the child should undergo a thorough medical and neurological examination. This should include CT brain scan, EEG, chromosome analysis, and screening for metabolic diseases and intrauterine **virus** infections. Sometimes examinations of liquor and auditory brain-stem responses are indicated.

L10 ANSWER 13 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1984:203295 BIOSIS
DN BA77:36279
TI AUTISM IN A CHILD WITH CONGENITAL CYTOMEGALOVIRUS INFECTION.
AU MARKOWITZ P I
CS DEP. PEDIATR., MED. COLL. VIRGINIA, BOX 487, RICHMOND, VIRGINIA 23298.
SO J AUTISM DEV DISORD, (1983) 13 (3), 249-254.
CODEN: JADDDQ.
FS BA; OLD
LA English
AB A case is reported of early infantile **autism** associated with a congenital cytomegalovirus infection. The **diagnosis** of **autism** is based on the child's failure to develop good interpersonal relationships, poor eye contact, delayed and deviant use of language and her rote and nonthematic use of objects and playthings. Resistance to change and self-stimulatory behavior were also present. Onset was before 2 yr of age. Congenital cytomegalovirus infection was suggested by the presence of an antibody response to the **virus**, culture of the **virus** from the urine, sensorineural hearing loss and inflammatory damage to the retina of the eye. Although over time improvement was noted, at last examination at the age of 5 yr her behavior is still markedly deviant. This and other reported cases suggest that congenital viral infection may be an important cause of infantile **autism**. It is hypothesized that an ability of the agent to establish chronic infection may predispose to behavioral aberration.

L10 ANSWER 15 OF 18 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 1998263515 EMBASE
TI Possible immunogenetic basis for autism.
AU Burger R.A.; Warren R.P.
CS R.A. Burger, Utah State University, Logan, UT 84322-6895, United States.
Roger@cpd2.usu.edu
SO Mental Retardation and Developmental Disabilities Research Reviews, (1998) 4/2 (137-141).
Refs: 28
ISSN: 1080-4013 CODEN: MRDRFI
CY United States
DT Journal; General Review
FS 022 Human Genetics
026 Immunology, Serology and Transplantation

032 Psychiatry

LA English

SL English

AB **Autism** results from several different etiologies or combination of pathological mechanisms. Mounting evidence indicates that immune dysfunction along with an environmental **pathogen** may be factors contributing to the development of some cases of **autism**. One of the immune deficiencies observed in **autism** is abnormal T-cell mediated immunity. Another is altered levels of certain classes of antibodies (immunoglobulins), including decreased levels of immunoglobulin A and deficient complement activity, based on the inheritance of a null allele of the C4B gene. In addition to the C4B gene, other genes on chromosome 6 also appear to be associated with **autism**. In the developing child, genetically **determined** immune deficiencies might increase the risk for **autism** in two ways: 1) A **pathogen** or its toxins might damage the brain, 2) the **pathogen** might trigger an autoimmune mechanism that would interfere with brain functioning. In the mother, immune deficiency might allow a **pathogen** to persist in utero, damaging the fetal brain directly or triggering a maternal immune response that creates pathogenesis in the fetal brain.

L12 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 2002:488136 CAPLUS
DN 137:30245
TI Methods for diagnosing pervasive development disorders, dysautonomia and other neurological conditions
IN Fallon, Joan M.
PA USA
SO U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002081628	A1	20020627	US 2001-990909	20011116
PRAI US 2000-249239P	P	20001116		

AB Methods for aiding in the **diagnosis** of disorders including, but not limited to, **PDDs** (Pervasive **Development Disorders**), Dysautonomic disorders, Parkinson's disease and SIDS (Sudden Infant Death Syndrome). In one aspect, a **diagnosis** method comprises analyzing a stool sample of an individual for the presence of a biol. marker (or marker compd.) comprising one or more **pathogens**, which provides an indication of whether the individual has, or can develop, a disorder including, but not limited to, a **PDD**, Dysautonomia, Parkinsons disease and SIDS. Preferably, the presence of one or more pathogens is detd. using a stool immunoassay to det. the presence of antigens in a stool sample, wherein such antigens are assocd. with one or more pathogens including, but not limited to, Giardia, Cryptosporidium, E. histolytica, C. difficile, Adenovirus, Rotavirus or H. pylori.

L13 10421 (DISEASE OR DISORDER) (S) (PLURAL### OR MULTIPL##### OR SEVERAL) (3A) (PATHOGEN OR BACTER### OR VIRUS## OR INFECT####)

L14 2799 L13 AND (DIAGNOS### OR DETERMIN#####) (S) (DISEASE OR DISORDER)

L15 2700 L13 AND ((DISEASE OR DISORDER) (S) (PLURAL### OR MULTIPL##### OR SEVERAL) (3A) (PATHOGEN OR BACTER### OR VIRUS## OR INFECT####)) (P) ((DIAGNOS### OR DETERMIN#####) (S) (DISEASE OR DISORDER))

L13 10421 S (DISEASE OR DISORDER) (S) (PLURAL### OR MULTIPL##### OR SEVER
L14 2799 S L13 AND (DIAGNOS### OR DETERMIN#####) (S) (DISEASE OR DISORDE
L15 2700 S L13 AND ((DISEASE OR DISORDER) (S) (PLURAL### OR MULTIPL#####
L16 1333 DUP REM L15 (1367 DUPLICATES REMOVED)
L17 1025 S L16 NOT PY>2000
L18 10 S L17 AND (HELICOBACTER OR PYLORI)

(DIAGNOS### OR DETERMIN#####) (S) (DISEASE OR DISORDER)

L18 ANSWER 3 OF 10 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:169707 BIOSIS
DN PREV200000169707
TI Patients with acute myocardial infarction in Northern Italy are often infected by **Helicobacter pylori**.
AU Pellicano, R.; Parravicini, P. P.; Bigi, R.; La Rovere, M. T.; Baduini, G.; Gandolfo, N.; Casaccia, M.; Reforzo, F.; Santoriello, L.; Aruta, E.; Marenco, G.; Arena, V.; Bazzoli, F.; Rizzetto, M.; Ponzetto, A. (1)
CS (1) UOA Gastroenterology, Molinette Hospital, Corso Bramante 88, 10126, Turin Italy
SO Panminerva Medica., (Dec., 1999) Vol. 41, No. 4, pp. 279-282. ISSN: 0031-0808.
DT Article
LA English
SL English
AB Background: The classical risk factors for acute myocardial infarction (AMI) fail to explain all the epidemiological variations of the **disease**. Among the new risk factors recently reported, **several infectious** agents appear to increase the risk of AMI. In particular, acute and chronic respiratory **diseases** due to Chlamydia pneumoniae, and **Helicobacter pylori** (H. **pylori**) infection seem to be strongly involved. The aim of this work is to **determine** the prevalence of H. **pylori** infection in a group of male patients with AMI, in a case-control study, where a group of blood donors matched for sex and age served as control. We searched for the classical risk factors in all patients. Methods: We studied 212 consecutive male patients, aged 40-65 years, admitted for AMI at the Coronary Care Units at Hospitals in three towns of Northern Italy. H. **pylori** infection was assessed by the highly specific and sensitive 13C-urea breath test and by presence of antibodies (IgG) against H. **pylori** in circulation. Volunteer blood donors attending our Hospital Blood Bank served as controls. Among the patients we investigated the presence of hypertension, cholesterol and glucose levels in serum, fibrinogen in plasma and the smoking habit. Results: H. **pylori** infection was present in 187/212 (88%) of the patients and in 183/310 (59%) of the control population ($p<0.0001$). Classical risk factors for AMI did not differ among patients with and without H. **pylori** infection. Conclusion: Patients admitted to the Coronary Care Unit for acute myocardial infarction had a notably higher prevalence of H. **pylori** infection than the general population. The classical risk factors for coronary **disease** were equally present in all patients with AMI irrespective of H. **pylori** status.

WEST Search History

DATE: Friday, July 11, 2003

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR		
L16	L14 and (pathogen or virus or bacter$4 or helicobacter or pylori) with autism	0	L16
L15	L14 and (pathogen or virus or bacter$4 or helicobacter or pylori) with (development$3 adj disorder or autism or PDD)	1	L15
L14	L13 not l4	155	L14
L13	L12 and l3	167	L13
L12	L11 or l8	580	L12
L11	L10 and l5	580	L11
L10	(pathogen or virus or bacter$4 or helicobacter or pylori) and (development$3 adj disorder or autism or PDD)	1449	L10
L9	L7 and developemental adj disorder	0	L9
L8	L7 and developmental adj disorder	150	L8
L7	L6 not l4	155	L7
L6	l3 and L5	167	L6
L5	(pathogen or virus or bacter$4 or helicobacter or pylori) and (developement$3 adj disorder or autism or PDD)	580	L5
L4	L3 and l2	12	L4
L3	(detect$5 or determin$5) with (pathogen or virus or bacter$4 or helicobacter or pylori) and (determin$5 or diagnos$3) with (developement adj disorder or autism or PDD)	167	L3
L2	(pathogen or virus or bacter$4 or helicobacter or pylori) same (developement adj disorder or autism or PDD)	106	L2
L1	(pathogen or virus or bacter$4 or helicobacter or pylori) and (developement adj disorder or autism or PDD)	580	L1

END OF SEARCH HISTORY

WEST Search History

DATE: Friday, July 11, 2003

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR		
L10	(disease or disorder) with (plural$4 or multipl$4) adj3 pathogen$2	44	L10
L9	L8 and l3	47	L9
L8	(plural$4 or multpl$5 or several) adj3 (antigen$2 or pathogen$2 or infect$5) same (diagnos$4 or determin$6) with (disease or disorder)	109	L8
L7	(plural$4 or multpl$5 or several) adj3 (antigen$2 or pathogen$2 or infect$5) same (diagnos$4 or determin$6 or disease oe disorder)	1349	L7
L6	l4 and l3	65	L6
L5	l4 and l3L4	0	L5
L4	l1 and (plural$4 or multpl$5 or several) adj3 (antigen$2 or pathogen$2 or infect$5)	145	L4
L3	L1 and @pd<20001116	170	L3
L2	L1 and @ad<20001116	254	L2
L1	(diagnos$3 or determin$6) with (disease or disorder) same (plural$4 or multpl$5 or several) with (antigen$2 or pathogen$2 or infect$5)	352	L1

END OF SEARCH HISTORY

STIC-ILL

NPL

From: STIC-Biotech/ChemLib
Sent: Friday, July 11, 2003 12:07 PM
To: STIC-ILL
Subject: FW: article request

Message to you.

-----Original Message-----
From: Lucas, Zacharia
Sent: Friday, July 11, 2003 11:55 AM
To: STIC-Biotech/ChemLib
Subject: article request

Examiner# : 79253 Zachariah Lucas
Art Unit : 1648
Phone Number: 308-4240
Date: 7-11-2003
Serial Number: 09/990909
MailBox & Bldg/Room Location: 8e12/8d16
Results Format Preferred (circle): Paper

Could you please send me a copy of the following article(s).

ARchives of Disease in Childhood, June 2001, 84(6): 525, articles by Richardson, and Murphy

Thank you,
Zac Lucas

LETTERS TO THE EDITOR

The discovery that *Helicobacter pylori* is the prime cause of peptic ulcer disease, is one of the most important advances in medicine in the 20th century. Subsequently, its importance in the causation of gastric cancer has been recognised. It is a rare cause of gastric lymphoma. Despite its significance as a pathogen, this organism colonises the gastric mucosa in up to 50 percent of the world's population. Not surprisingly research interest is intense. There has been much speculation (though little proof) that it might have a role in various other gastrointestinal and non-gastrointestinal disorders, including failure-to-thrive in infancy, short stature, anaemia, and even cardiovascular disease. Now a link has been proposed between *H pylori* and sudden infant death syndrome (SIDS). Recently, Kerr *et al* examined gastric, tracheal, and pulmonary tissue, looking for evidence of *H pylori* in SIDS victims and controls.[1] Based on polymerase chain reaction (PCR) techniques, they reported a highly significant association between SIDS and the presence of two *H pylori* genes (UreC, cagA) in these tissues. Not surprisingly, this reported association has evoked a lively correspondence. Important questions have been raised regarding both methodology and interpretation.

M STEPHEN MURPHY
Associate Editor

1 Kerr JR, Al-Khattaf A, Barson AJ, *et al*. An association between sudden infant death syndrome (SIDS) and Helicobacter pylori infection. *Arch Dis Child* 2000;83:429–34.

Association between SIDS and *H pylori* infection

EDITOR,—The article in the November issue of the *Archives* on the association between sudden infant death syndrome (SIDS) and *H pylori* infection is confusing.[1] I am very familiar with *H pylori* colonisation in gastric biopsies in children and its association with gastritis, peptic ulcer, and gastric cancer. However, the implication that the organism can cause an unexpected infant death that is, SIDS, is shocking!

Unexplained infant deaths (SIDS) are "fertile soil" for speculators that apply new technology polymerase chain reaction (PCR) to uncover new associations. Unfortunately, these observations are not based on an infrastructure of knowledge of the causes of infant mortality. Caution needs to be exercised when applying PCR technology to postmortem tissue and "discovering" an answer. The possibility of contamination is real, and in addition infants can die with something, and not of it.

I would value a response from Drs Fleming, Blair, Bacon, and Berry who co-authored the CESDI study of SUDI.

RALPH A FRANCIOSI
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Children's Hospital and Medical College of Wisconsin,
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ralphii@mcw.edu

1 Kerr JR, Al-Khattaf A, Barson AJ, *et al*. An association between sudden infant death syndrome (SIDS) and Helicobacter pylori infection. *Arch Dis Child* 2000;83:429–34.

Ammonia—not the culprit

EDITOR,—We were interested to read the article by Kerr *et al* on the SIDS problem. With regard to the interesting results we would like to point out some related findings. As pointed out by Kerr *et al*, *H pylori* is abundant in less advantageous parts of society where smoking is often frequent, and sometimes where SIDS occurs. The fact that smoking is often inversely related to the ability of *H pylori* to colonise and to be transmitted from mother to child[2] might indicate that it is sensitive to smoke itself, or products generated after smoke inhalation. It is interesting to note that endogenous products of smoke, like nitrate and nitrite, often inhibit bacterial growth.[3 4]

Furthermore, we have previously shown that total breakdown of all ingested urea takes place in all normal infants without causing problems of ammonia intoxication.[5] This is in contrast to SIDS victims, most of whom have unmetabolised urea in their faeces.[5] Due to these related circumstances it may seem a little adventurous to suggest that ammonia produced by *H pylori* could cause death in SIDS.

LARS WIKLUND
GUNNAR RONQUIST
MARY GEORGE
Department of Anaesthesia,
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Control your controls and conclusions

EDITOR,—In a retrospective study, Kerr and coworkers investigated formalin fixed, paraffin embedded tissues (stomach, trachea, and lung) of 32 infants who had died of SIDS, and eight control cases, with nested polymerase chain reaction (PCR) and ELISA of the amplicons. A child was considered as infected with *H pylori* if the optical density of the ELISA was above the mean value plus 2 SD obtained in the tissue of control infants. The authors found that 28 of the 32 SIDS cases, but only one of the eight control cases fulfilled these criteria. They conclude from their results that *H pylori* infection may play a causative role in SIDS. We have serious doubts about their results and conclusions.

The control group was extremely small in size and we would expect most, if not all, of these eight infants to have received one or more antibiotics in high doses intravenously over several days before death, as the causes of death were bacterial meningitis, septicaemia, pneumonia, necrotising enterocolitis, ileal perforation, and prematurity. In contrast, few if any of the SIDS victims would have received intravenous antibiotics. Therefore, if control children had been colonised with *H pylori*, the bacteria may have been suppressed. These eight infants are certainly not appropriate controls for this kind of study.

Nested PCR is a very sensitive method with a high risk of false positive results caused by contamination. The applied ELISA is yet another amplifying method which also increases the risks of unspecific binding. Although the authors stated that they tried to minimise contamination, no precautions have been performed at the time of autopsy and preservation of the tissue due to the retrospective character of the study. Because of the low specificity of the methods used, it is mandatory to prove the identity of the PCR amplicons as *H pylori* specific by sequencing the products. Such confirmation is not reported in the paper. To show the specificity of their method, the authors could have also performed analyses on control tissues—for example, brain, which are unlikely to be *H pylori* infected even when other tissues were assessed as "positive".

The fact that *H pylori* was not shown in the stomach, trachea, or lung by histology in any of the children must raise major concerns that the applied methods were not specific. Other methods for detection of *H pylori* infection like fluorescence in situ hybridisation (FISH) have not been applied.[1] The authors do not report whether any of the children had histological signs of acute or chronic gastritis, which is found even in young children with *H pylori* infection.[2] If the bacterial load was so small that neither the bacteria nor the associated inflammation could be detected by histology, it seems questionable that metabolic products produced by *H pylori* (or example, ammonia, may play a causative role as a cause of SIDS as suggested by the authors.

Finally, the authors mention that both *H pylori* infection and SIDS are more common in poor socioeconomic populations but fail to provide any information on the ethnic and socioeconomic background of their cases and control infants. From many epidemiologic studies and our own experience, it seems extremely unlikely that 28 of 32 infants (87%) under 28 weeks of age are infected by *H pylori* in a country such as the UK, unless these children are from immigrant groups. We are, for example, following a cohort of German children from birth with regular testing for *H pylori* infection by two non-invasive tests: the detection of *H pylori* antigen in stool (HpSA, Meridian Diagnostics, Cincinnati, USA) and the ^{13}C-urea breath test corrected for estimated individual CO_2 production rate.[4] Although a quarter of the children have at least one *H pylori* infected parent (positive serology and/or a positive ^{13}C-urea breath test) only 1.5% of the children have positive tests during the first three years of age.

On publication, this paper was widely reported by the media, a process actively assisted by the authors. This is likely to result in considerable anxiety among young parents and pregnant women, feelings of guilt in parents of SIDS children and unjustified *H pylori*